Cleavage of Carbon−Carbon Triple Bond of Alkyne via Hydroiminoacylation by Rh(I) Catalyst

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The cleavage of carbon−carbon bonds has become one of the most challenging subjects in organic chemistry.[1] Despite remarkable progress in this area, alkyne cleavage has been demonstrated only on a few examples including alkyne-ligand scission on metal complexes[2] and oxidative cleavage[3] in addition to alkyne metathesis.[4] Moreover, most of them are not efficient enough to be utilized for synthetic purpose. Therefore, we attempted to develop a catalytic process to cleave C−C triple bonds by utilizing our chelation-assisted hydroacylation methodology established in pursuit of C−H and C−C bond activation.[5,6] Described herein is a novel one-pot protocol for the catalytic cleavage of C−C triple bonds through hydroiminoacylation of alkyne followed by amine-assisted C−C double bond cleavage of the resulting α,β-unsaturated ketimine. As in the schematic representation (Scheme 1), the C−C triple bond of alkyne **2** is divided into (i) an aldehyde and (ii) the alkylmethylene unit of ketone **3** formed by the combination of allylamine **1**, an acyl equivalent.

When the reaction of allylamine **1a** and 2-butyne (**2a**, 1.2 equiv of **1a**) was carried out at 130 °C for 12 h in the presence of Rh(PPh$_3$)$_3$Cl (**4**, 3 mol %), cyclohexylamine (**5**, 200 mol %) and benzoic acid (**6**, 5 mol %), ketimine **7a** was determined in a quantitative yield by GC analysis along with aldimine **8a** (eq 1). Hydrolysis of imine **7a** gave 1-phenyl-pentan-3-one (**3a**) in a 98% isolated yield.[7] Eventually, both ethylidene moiety of aldimine **8a** and ethyl group of ketimine **7a** were derived from the C−C triple bond cleavage of 2-butyne (**2a**). This C−C bond cleavage was investigated with a variety of symmetric alkynes **2** including aliphatic and aromatic alkynes as shown in Table 1.[8] And

Scheme 1

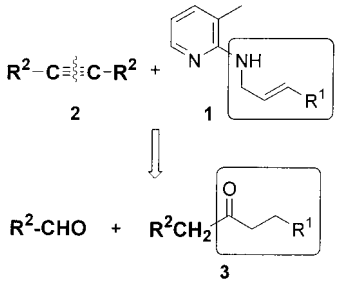
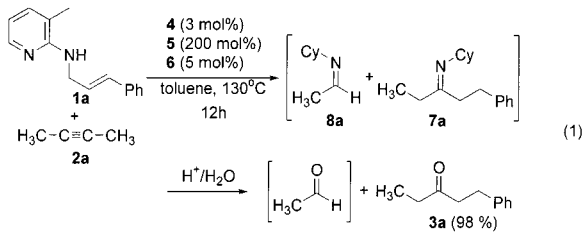


Table 1. The C−C triple bond cleavage of alkynes

entry	allylamine (**1**)	alkyne (**2**)	isolated yield (%)
1	**1a** (R^1 = Ph)	**2a** (R^2 = CH_3)	98 (**3a**)
2	**1a** (R^1 = Ph)	**2b** (R^2 = *n*-C_3H_7)	84 (**3b**)
3	**1a** (R^1 = Ph)	**2c** (R^2 = *n*-C_2H_5)	93 (**3c**)
4	**1a** (R^1 = Ph)	**2d** (R^2 = *n*-C_5H_{11})	91 (**3d**)
5	**1a** (R^1 = Ph)	**2e** (R^2 = Ph)	98[a] (**3e**)
6	**1b** (R^1 = CH_3)	**2b** (R^2 = *n*-C_3H_7)	80[b] (**3f**)
7	**1b** (R^1 = CH_3)	**2e** (R^2 = Ph)	94[a] (**3g**)
8	**1c** (R^1 = H)	**2e** (R^2 = Ph)	92[a] (**3h**)

[a] The reaction was carried out with **6**. [b] GC yield.

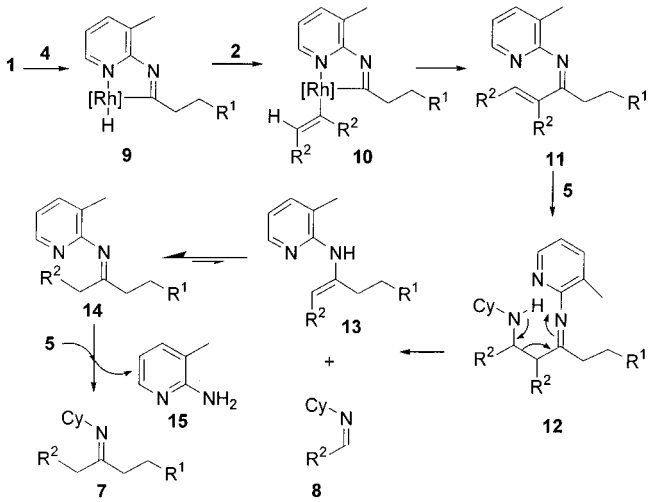
crotylamine **1b** and allylamine **1c** were used in addition to 3-phenylallylamine **1a**. All reactions exhibited fairly good yields (80−98%) of the corresponding alkyne cleavage product **3**.



(1)

The mechanism of this transformation is proposed as in Scheme 2. The first step should be the isomerization of allylamine **1** to

Scheme 2. Plausible Mechanism for Triple Bond Cleavage of Alkyne



aldimine, followed by a C−H bond cleavage of aldimine by Rh(I) to yield iminoacylrhodium(III) hydride **9**.[9] The hydrometalation

(1) For reviews, see: (a) Rybtchinski, B.; Milstein, D. *Angew. Chem., Int. Ed.* **1999**, *38*, 870. (b) Jennings, P. W.; Johnson, L. L. *Chem. Rev.* **1994**, *94*, 2241. (c) Crabtree, R. H. *Chem. Rev.* **1985**, *85*, 245. (d) Murakami, M.; Ito, Y. In *Activation of Unreactive Bonds and Organic Synthesis*; Murai, S. Ed.; Springer: Berlin, 1999; pp 97−129.

(2) (a) Morris, M. J. In *Metal Clusters in Chemistry;* Braunstein, P., Oro, L. A., Raithby, P. R., Eds.; Wiley-VCH: Weinheim, 1999; Vol. 1; pp 221−235. (b) Cairns, G. A.; Carr, N.; Green. M.; Mahon, M. F. *Chem. Commun.* **1996**, 2431. (c) O'Connor, J. M.; Pu, L. *J. Am. Chem. Soc.* **1990**, *112*, 9013. (d) Degani, Y.; Willner, I. *J. Chem. Soc., Chem. Commun.* **1985**, 648. (e) Sullivan B. P.; Smythe, R. S.; Kober, E. M.; Meyer, T. J. *J. Am. Chem. Soc.* **1982**, *104*, 4701. (f) Hayashi, N.; Ho, D. M.; Pascal, R. A., Jr. *Tetrahedron Lett.* **2000**, *41*, 4261.

(3) (a) Moriarty, R. M.; Penmasta, R.; Awasthi, A. K.; Prakash, I. *J. Org. Chem.* **1988**, *53*, 6124. (b) Sawaki, Y.; Inoue, H.; Ogata, Y. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 1133.

(4) (a) For a review, see: Bunz, U. H. F.; Kloppenburg, L. *Angew. Chem., Int. Ed.* **1999**, *38*, 478. (b) Fürstner, A.; Grela. K.; Mathes, C.; Lehmann, C. W. *J. Am. Chem. Soc.* **2000**, *122*, 11799. (c) Fürstner, A.; Mathes, C.; Lehmann, C. W. *J. Am. Chem. Soc.* **1999**, *121*, 9453. (d) Fürstner, A.; Seidel, G. *Angew. Chem., Int. Ed.* **1998**, *37*, 1734. (e) Kloppenburg, L.; Song, D.; Bunz, U. H. F. *J. Am. Chem. Soc.* **1998**, *120*, 7973. (f) McCullough, G. L.; Schrock, R. R. *J. Am. Chem. Soc.* **1984**, *106*, 4067. (g) Montreux, A.; Blanchard, M. *J. Chem. Soc., Chem. Commun.* **1974**, 786.

(5) For C−H bond activation, see: (a) Jun, C.-H.; Lee, D.-Y.; Lee, H.; Hong, J.-B. *Angew. Chem., Int. Ed.* **2000**, *39*, 3070. (b) Jun, C.-H.; Lee, H.; Hong, J.-B. *J. Org. Chem.* **1997**, *62*, 1200. (c) Jun, C.-H.; Lee, D.-Y.; Hong, J.-B. *Tetrahedron Lett.* **1997**, *38*, 6673.

(6) For C−C bond activation, see: (a) Jun, C.-H.; Lee, H.; Lim, S.-G. *J. Am. Chem. Soc.* **2001**, *123*, 751. (b) Jun, C.-H.; Lee, H. *J. Am. Chem. Soc.* **1999**, *121*, 880.

(7) Acetaldehyde generated from hydrolysis of aldimine **8a** was evaporated during isolation.

(8) With a terminal alkyne, no desired product was observed, due to its extremely poor reactivity to hydroiminoacylation with allylamine **1**.

(9) Jun, C.-H.; Lee, H.; Park. J.-B.; Lee, D.-Y. *Org. Lett.* **1999**, *1*, 2161.

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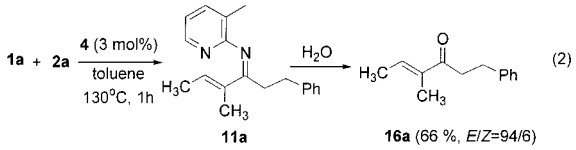
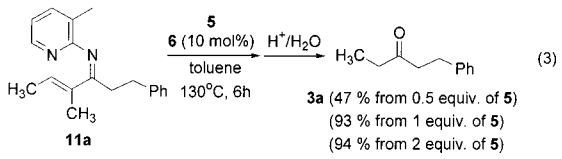
of **9** into alkyne **2** and the reductive elimination of the resulting iminoacylrhodium(III) vinyl complex **10** afford (*E*)-α,*β*-unsaturated ketimine **11**. A conjugate addition of cyclohexylamine (**5**) into the α,*β*-unsaturated ketimine **11** proceeds to form a *β*-aminoketimine **12**. The retro-Mannich type fragmentation of **12** affords enamine **13** and aldimine **8**.[10] Enamine **13** is isomerized to ketimine **14**, which is transiminated by **5** to ketimine **7** with liberating 2-amino-3-picoline (**15**).[11]

To clarify the proposed mechanism, the following experiments were performed: the formation of α,*β*-unsaturated ketimine **11** from **1** and **2**, and the transformation of **11** to **7**. When the reaction of **1a** and **2a** was carried out at 130 °C for 1 h in the presence of **4** (3 mol %) without cyclohexylamine (**5**) and benzoic acid (**6**), a hydroiminoacylated product of 2-butyne, **11a**, was obtained in a quantitative yield by GC analysis (eq 2). After hydrolysis of **11a**,[12] α,*β*-unsaturated ketone **16a** was isolated in a 66% yield (*E*/*Z* = 94/6).[13] The formation of *E*-**16a** was predominated by *syn*-addition of **9**.



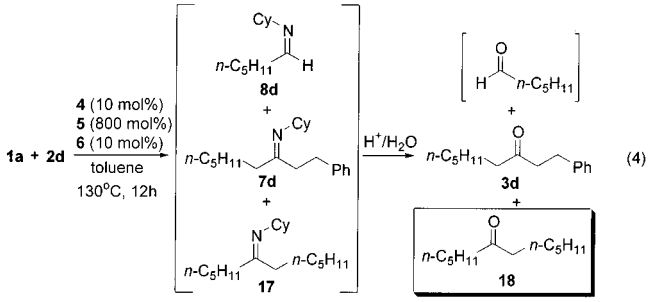
(2)

When ketimine **11a** was allowed to react with 0.5 equiv of **5** in the presence of benzoic acid (**6**, 10 mol % based on **11a**) at 130 °C for 6 h, a 47% yield of **3a** was obtained upon hydrolysis. As the amount of **5** was increased to a 1−2 equiv, an almost complete conversion (93 and 94% GC yield) of **11a** to **3a** was observed. These results imply that one equivalent of **5** is enough to cleave a C−C double bond of **11** to yield **13** and **8** through the intermediate *β*-aminoketimine **12**.



(3)

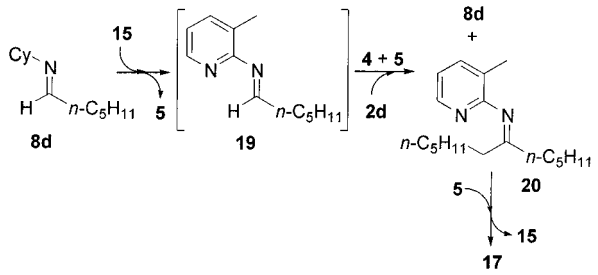
Imine **8** may undergo another hydroiminoacylation as long as enough alkyne exists. When allylamine **1a** was treated with a large excess of 6-dodecyne (**2d**) (8 equiv of **1a**) in the presence of **4** (10 mol %), **5** (800 mol %), and **6** (10 mol %), a 1:1.2 mixture of 1-phenyl-nonan-3-one (**3d**) and 6-dodecanone (**18**) was determined by GC analysis after hydrolysis (eq 4).[14] Newly formed ketone **18** is assumed to be produced by hydrolysis of imine **17** generated from the reaction of **8d** with the remaining alkyne **2d**.



(4)

The mechanism for the conversion of **8d** to **17** is depicted in Scheme 3. The hexanal imine **8d** is transiminated by 2-amino-3-picoline (**15**) to yield aldimine **19**. At this stage, imine **19** would be subject to the present alkyne cleavage sequence with **2d** to produce ketimine **20** with regeneration of imine **8d**, the starting material of this transformation. Then, the resulting imine **20** is transiminated by **5** to give **17** with liberation of **15**.

Scheme 3



In conclusion, a carbon−carbon triple bond cleavage of alkyne was accomplished under the catalytic system consisting of Rh(I) complex, cyclohexylamine, and benzoic acid. This one-pot protocol is realized by a tandem reaction, which is composed of hydroiminoacylation of alkyne with an allylamine derivative by Rh(I) catalyst, a conjugate addition of cyclohexylamine into the resulting α,*β*-unsaturated ketimine, and a subsequent retro-Mannich type fragmentation. Further study toward synthetic application of this method is under investigation.

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Supporting Information Available: Experimental procedures for the catalytic C−C triple bond cleavage of 2-butyne (**2a**) with allylamine **1a** by **4**, **5**, and **6**, the hydroiminoacylation of **2a** with **1a** by **4**, and retro-Mannich type fragmentation of α,*β*-unsaturated ketimine including the characterization data for **7a**, **11a**, and **16a** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA011053Z

(10) For the fragmentation of α,*β*-unsaturated ketone, see: (a) Kondo, Y.; Kon-i, K.; Iwasaki, A.; Ooi, T.; Maruoka, K. *Angew. Chem., Int. Ed.* **2000**, *39*, 414. (b) Eisch, J. J.; Sanchez, R. *J. Org. Chem.* **1986**, *51*, 1848. (c) Hanquet, B.; Borai, M. E.; Guilard, R. *Tetrahedron Lett.* **1982**, *23*, 2859. (d) Jensen, J. L.; Hashtroudi, H. *J. Org. Chem.* **1976**, *41*, 3299. (e) Nielsen, A. T.; Haseltine, S. *J. Org. Chem.* **1968**, *33*, 3264.

(11) Jun, C.-H.; Hong. J.-B. *Org. Lett.* **1999**, *1*, 887.

(12) Ketimine **11a** is so stable as to be hydrolyzed only by Rh(I) complex and H_2O at 130 °C.

(13) For direct hydroacylation of alkyne, see: (a) Kokubo, K.; Matsumasa, K.; Miura, M.; Nomura, M. *J. Org. Chem.* **1997**, *62*, 4564. (b) Lee, H.; Jun, C.-H. *Bull. Korean Chem. Soc.* **1995**, *16*, 1135. (c) Tsuda, T.; Kiyoi, T.; Saegusa, T. *J. Org. Chem.* **1990**, *55*, 2554.

(14) For the isolation of **18**, 6-dodecyne (**2d**) was used instead of 2-butyne (**2a**). **3d** and **17** were isolated in 25 and 31% yields, respectively. Hexanal generated from hydrolysis of **8d** was not isolated.